Citation:

Shea MK, Houston DK, Nicklas BJ, Messier SP, Davis CC, Miller ME, Harris TB, Kitzman DW, Kennedy K, Kritchevsky. The effect of randomization to weight loss on total mortality in older overweight and obese adults: The ADAPT study. *J of Gerontol A Biol Sci Med Sci* 2010; 65: 519-525.

PubMed ID: 20080875

Study Design:

Randomized Controlled Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine whether randomization to a weight reduction program was associated with total mortality in overweight and obese older adults.

Inclusion Criteria:

All participants in the Arthritis, Diet and Activity Promotion Trial (ADAPT); inclusion criteria for ADAPT:

- Age≥60 years
- BMI≥28.0kg/m^2
- Has knee osteoarthritis (radiographic evidence of grade I-III tibiofemoral or patellofemoral OA based on weight-bearing anteroposterior and sunrise view radiographs)
- Sedentary activity pattern with<20 minutes of formal exercise once weekly for the six months prior to enrollment.
- Knee pain on most days
- Self-reported difficulty in at least one of the following activities ascribed to knee pain:
    - Walking one-quarter of a mile (three to four city blocks)
    - Climbing stairs
    - Bending
    - Stooping
    - Kneeling (e.g., to pick up clothes)
    - Shopping
    - House cleaning or other self-care activities:
        - Getting in and out of bed
        - Standing up from a chair
        - Lifting and carrying groceries
        - Getting in and out of the bathtub.

Exclusion Criteria:

- Serious medical condition that prevented safe participation in an exercise program, including symptomatic heart or vascular disease (angina, peripheral vascular disease, congestive heart failure), severe hypertension, recent stroke, chronic obstructive pulmonary disease, severe insulin-dependent diabetes mellitus, psychiatric disease, renal disease, liver disease, active cancer other than skin cancer and anemia
- A Mini-Mental State Examination score of <24
- Inability to walk without a cane or other assistive device
- Reported alcohol consumption of >14 drinks per week
- ST segment depression of at least 2mm at an exercise level of 4 METS or less, hypotension, or complex arrhythmias during a graded exercise test.

Description of Study Protocol:

Recruitment

Volunteers were all participants in the ADAPT trial. Volunteers for the ADAPT trial were recruited from North Carolina over an 18-month period. Mass mailings, presentations, mass media advertisements and print advertising were used for recruiting.

Design

Randomized controlled trial with prospective follow-up. Volunteers were randomized into one of four intervention groups (see below). Each intervention lasted 18 months; volunteers were then followed until death or for up to 10 years in order to assess mortality rate.

Dietary Intake/Dietary Assessment Methodology

Not applicable

Blinding used

Determination and verification of death was completed without knowledge of randomization group.

Intervention

- Dietary weight loss: 18 total months in which social cognitive theory principles were utilized to help participants cut energy intake in order to lose at least 5% of initial body weight
- Exercise alone: Three days per week for 18 months of a prescribed exercise program consisting of 30 minutes aerobic exercise plus 15 minutes resistance training plus 15 minutes cool down
- Dietary weight loss plus exercise: Combination of dietary weight loss and exercise programs
- Healthy lifestyle control: Attended three group educational sessions on osteoarthritis, obesity and exercise during months one to three, followed by monthly phone contact during months four to six and bi-monthly phone contact for months seven to 18.

Statistical Analysis

- The four randomization groups were combined into two groups for analysis: "weight loss intervention" combined the dietary weight loss and dietary weight loss plus exercise groups. "Non-weight loss intervention" combined the exercise alone and healthy lifestyle control groups.
- Cox proportional hazard regression with multivariate adjustments used to determine hazard ratios for total mortality rate.

Data Collection Summary:

Timing of Measurements

- BMI was calculated from measured height and weight at baseline and 18 months
- Determination of death was conducted from baseline (between 11/1996 and 6/1998) through 12/31/2006.

Dependent Variables

Death; ascertained using the Social Security Index and the National Death Index.

Independent Variables

- "Weight loss intervention group" or "non-weight loss intervention group." Weight loss intervention group combined all ADAPT participants randomized to the dietary weight loss and dietary weight loss plus exercise groups. Non-weight loss intervention group combined all ADAPT participants randomized to the exercise alone and healthy lifestyle control groups.

Control Variables

- Age
- Sex
- BMI calculated from measured height and weight at baseline
- Weight change and percent weight loss calculated using measured body weight at baseline and 18 months.
- Exercise treatment, defined as randomization into the exercise alone or dietary weight loss plus exercise groups.

Description of Actual Data Sample:

- *Initial N:* 318
    - 228 females
    - 90 males
- *Attrition (final N):* 318
    - 228 females
    - 90 males used for intent-to-treat analysis; N=316 for stratified analyses
        - Weight loss intervention group: N=159
            - 115 females
            - 44 males; N=158 for stratified analyses
        - Non-weight loss intervention group: N=159

- 113 females
- 46 males; N=158 for stratified analyses

- *Age:* (mean±SD); overall mean=68.5 years
  - Weight loss intervention group: 68.2±6.1 years
  - Non-weight loss intervention group: 69.0±6.3 years
- *Ethnicity:* White: N=241
- *Other relevant demographics:*
  - Coronary heart disease:
    - Weight loss intervention group, N=65
    - Non-weight loss intervention group, N=77
  - Diabetes:
    - Weight loss intervention group, N=15
    - Non-weight loss intervention group, N=17
- *Anthropometrics:* (mean±SD)
  - Weight loss intervention group:
    - Baseline BMI 34.3±5.3kg/m^2
    - Baseline weight 93.6±16.2kg
  - Non-weight loss intervention group:
    - Baseline BMI 34.2±4.9kg/m^2
    - Baseline weight 93.9±16.9kg
- *Location:* North Carolina.

Summary of Results:

Table 1: Weight Loss and Mortality Rate in Volunteers Randomized to a Weight Loss Intervention or Non-weight Loss Intervention.

	Weight Loss Intervention Group	Non-weight Loss Intervention Group	P-value
Deaths (N)	15	30	
Six-month weight loss (kg)[1]	4.4±5.3	0.3±3.0	<0.01
18-month weight loss (kg)	4.8±7.5	1.4±5.1	<0.01
Unadjusted mortality rate[2] (HR [95%CI])	0.5 [0.3-0.9]	1	0.01
Adjusted mortality rate[1,3] (HR [95%CI])	0.5 [0.3-1.0]	1	0.03

- [1]N=316; [2]N=318; [3]adjusted for age, sex and exercise treatment
- Weight loss intervention group lost more weight during treatment and demonstrated a lower rate of all-cause mortality during 10 years of follow-up.

Table 2: Adjusted Rates of Total Mortality Among Volunteers Randomized to a Weight-loss Intervention or a Non-weight Loss Intervention Stratified on Potential Confounding Variables.

	Weight Loss Intervention Group; HR (95% CI)	Non-weight Loss Intervention Group
Baseline BMI≤33.5kg/m^2	0.5 (0.2-1.1)	1
Baseline BMI >33.5kg/m	0.5 (0.2-1.5)	1
≤67.1 years	0.7 (0.2-2.4)	1
>67.1 years	0.5 (0.2-1.0)	1
Males	0.5 (0.2-1.4)	1
Females	0.5 (0.2-1.2)	1
At least two years follow-up	0.5 (0.3-1.0)	

- Among individuals who were older at baseline than the baseline median age (67.1 years), those in the weight-loss intervention group had a lower mortality rate than those in the non-weight loss intervention group
- Among individuals who had more than two years of follow-up, those in the weight-loss intervention group had a lower mortality rate than those in the non-weight loss intervention group.

Other Findings

- Within the weight loss intervention group, mortality rate was not different in individuals who lost more than the median of body weight loss (3.6kg) compared to those who lost less; HR [95% CI] 1.2 [0.3-4.6)
- Within the weight loss intervention group, mortality rate was not different in individuals who lost at least 5% of initial body weight compared to those who lost less; HR [95% CI] 1.5 [0.4-5.5)
- Randomization to one of the two exercise interventions did not increase mortality rate; HR [95% CI] 1.3 (0.7-2.2).

Author Conclusion:

Modest intentional weight loss does not increase risk for all-cause mortality in overweight older adults, but rather may reduce mortality risk over the long-term.

Reviewer Comments:

- *Sample size was small and number of deaths in the weight loss intervention group minimal*
- *Selection of volunteers was biased; limited to older, overweight adults with osteoarthritis which may not represent the entire population of overweight, older adults*
- *Reason of death was not ascertained; therefore, no attempt was made to separate individuals who may died from health reasons vs. those who died from non-health related incidents. Weight loss intent is not likely to have an effect on mortality rate from non-health related incidents (e.g., car accident).*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	Yes
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes

3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	???
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A

6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	N/A
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	No
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	Yes
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	???
8.6.	Was clinical significance as well as statistical significance reported?	Yes

8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes